

What is Claimed is:

1. A method of eliciting a TLR8-mediated cellular response in a cell that expresses TLR8 comprising:

5 selecting a compound identified as a TLR8 agonist; and
 administering to the cell the compound in an amount that affects at least one
 TLR8-mediated cellular signaling pathway;

10 wherein the TLR8 agonist is a substituted imidazoquinoline amine; a
 tetrahydroimidazoquinoline amine; an imidazopyridine amine; a 1,2-bridged
 imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an
 imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an
 oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a
 thiazolopyridine amine; an oxazolonaphthyridine amine; a thiazolonaphthyridine
 amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-
15 imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine,
 naphthyridine amine, or tetrahydronaphthyridine amine.

2. The method of claim 1 wherein the cell is a monocyte, a macrophage, a
dendritic cell, a B lymphocyte, a Natural Killer cell, a polymorphonuclear cell, or a cell
20 derived from any of the foregoing.

3. The method of claim 1 wherein the cellular response comprises NF- κ B
activation, production of at least one cytokine, production of at least one co-stimulatory
marker, or any combination thereof.

25 4. A method of treating an organism having a condition treatable by modulating a
 TLR8-mediated cellular response comprising:

 selecting a compound identified as a TLR8 agonist; and
 administering to the organism the compound in an amount effective to modulate
30 a TLR8-mediated cellular signaling pathway;
 wherein the TLR8 agonist is a substituted imidazoquinoline amine; a
 tetrahydroimidazoquinoline amine; an imidazopyridine amine; a 1,2-bridged
 imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an

imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an oxazolonaphthyridine amine; a thiazolonaphthyridine amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine, naphthyridine amine, or tetrahydronaphthyridine amine.

5. The method of claim 4 wherein the organism is a mammal.

10 6. The method of claim 5 wherein the mammal is a human.

7. The method of claim 6 wherein the condition is a neoplastic disease.

8. The method of claim 6 wherein the condition is a T_H2-mediated disease.

15 9. The method of claim 8 wherein the condition is asthma, allergic rhinitis, or atopic dermatitis.

20 10. The method of claim 6 wherein the condition is a viral disease, a bacterial disease, a parasitic disease, a protozoal disease, or a prion-mediated disease.

25 11. The method of claim 4 wherein administering the IRM compound modulates NF- κ B activity, the production of at least one cytokine, the production of at least one co-stimulatory marker, the production of an intercellular adhesion molecules, the production of a maturation marker, or any combination thereof.

12. A method of identifying a TLR8 agonist comprising:

- a) exposing a TLR8-positive cell culture to a test compound and measuring a TLR8-mediated cellular response;
- 30 b) exposing a TLR8-negative cell culture to a test compound and measuring a TLR8-mediated cellular response; and

c) identifying the test compound as a TLR8 agonist if the cellular response in the TLR8-positive cell culture is greater than the cellular response of the TLR8-negative cell culture.

5 13. The method of claim 12 wherein the TLR8-negative cell culture comprises cells that express a dominant negative variant of TLR8.

14. The method of claim 12 wherein the TLR8-negative cell culture comprises antibodies raised against TLR8.

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15. The method of claim 12 wherein the TLR8-positive cell culture comprises cells that overexpress TLR8.

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16. The method of claim 12 wherein the test compound is identified as a TLR8 agonist if the cellular response of the TLR8-positive cell culture is at least 20% greater than the cellular response of the TLR8-negative cell culture.

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17. The method of claim 12 wherein the test compound is identified as an TLR8 agonist if the cellular response of the TLR8-positive cell culture is at least 50% greater than the cellular response of the TLR8-negative cell culture.

18. The method of claim 12 wherein the test compound is identified as a TLR8 agonist if the cellular response of the TLR8-positive cell culture is at least 80% greater than the cellular response of the TLR8-negative cell culture.

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19. The method of claim 12 wherein the TLR8-mediated cellular response comprises NF- κ B activation, the production of at least one cytokine, the production of at least one co-stimulatory marker or any combination thereof.

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20. A compound identified as a TLR8 agonist by the method of claim 12.

21. A pharmaceutical composition comprising a TLR8 agonist in combination with a pharmaceutically acceptable carrier.

22. A method of identifying an TLR8 antagonist comprising:

- a) exposing a first IRM-responsive cell culture to a TLR8 agonist and measuring a TLR8-mediated cellular response;
- 5 b) exposing a second IRM-responsive cell culture to a TLR8 agonist and a test compound, and measuring a TLR8-mediated cellular response; and
- c) identifying the test compound as an TLR8 antagonist if the cellular response in the first cell culture is greater than the cellular response of the second cell culture.

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23. The method of claim 22 wherein the TLR8 agonist is a substituted imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazopyridine amine; a 1,2-bridged imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an 15 oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an oxazolonaphthyridine amine; a thiazolonaphthyridine amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine, naphthyridine amine, or tetrahydronaphthyridine amine.

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24. A compound identified as a TLR8 antagonist by the method of claim 22.

25. A pharmaceutical composition comprising a TLR8 antagonist in combination with a pharmaceutically acceptable carrier.

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26. The use of a dominant-negative variant of TLR8 to identify a compound that activates a TLR8-mediated cellular signaling pathway.

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27. The use of an IRM compound as a positive control in an assay detecting activation of TLR8, wherein the IRM compound comprises a substituted imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an

oxazolonaphthyridine amine; a thiazolonaphthyridine amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine, naphthyridine amine, or tetrahydronaphthyridine amine.

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28. A method of eliciting a TLR8-mediated cellular response in a cell that expresses TLR8 comprising:

selecting a compound identified as a TLR8 antagonist; and
administering to the cell the compound in an amount that affects at least one

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TLR8-mediated cellular signaling pathway;

wherein the TLR8 antagonist is a substituted imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazopyridine amine; a 1,2-bridged imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an oxazolonaphthyridine amine; a thiazolonaphthyridine amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine, naphthyridine amine, or tetrahydronaphthyridine amine.

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29. A method of treating an organism having a condition treatable by modulating a TLR8-mediated cellular response comprising:

selecting a compound identified as a TLR8 antagonist; and

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administering to the organism the compound in an amount effective to modulate a TLR8-mediated cellular signaling pathway;

wherein the TLR8 antagonist is a substituted imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazopyridine amine; a 1,2-bridged imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an

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oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an oxazolonaphthyridine amine; a thiazolonaphthyridine amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-

imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine, naphthyridine amine, or tetrahydronaphthyridine amine.